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ABSTRACT

The Food Quality Protection Act of 1996 (FQPA) requires that the Environmental Protection Agency (EPA), which regulates the use of pesticides at the federal level, reevaluate the amounts of pesticide residues allowed on or in food. The EPA immediately began efforts to consider the additional safety factor for children, using available methods and data in an interim approach that has evolved over time. An internal committee now recommends whether to apply the additional safety factor in pesticide reviews, based on data completeness and evidence of increased susceptibility in children. Using this approach, the EPA has made decisions about applying the additional safety factor for 105 of the more than 450 pesticides to be reassessed. It determined that an additional safety factor was necessary in 49 cases and not necessary in the remaining 56 cases. Appendices contain the study methodology and evaluations of three pesticides evaluated under FQPA's new requirement for dicofol, methomyl, and phosmet. (DFR)

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GAO

Report to Congressional Requesters

September 2000

CHILDREN AND PESTICIDES

New Approach to Considering Risk Is Partly in Place

ED 448 533

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Abbreviations

EPA	Environmental Protection Agency
FQPA	Food Quality Protection Act of 1996
ILSI	International Life Sciences Institute
OPP	Office of Pesticide Programs

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United States General Accounting Office
Washington, D.C. 20548

Health, Education, and
Human Services Division

B-284334

September 11, 2000

The Honorable Edward M. Kennedy
The Honorable Barbara A. Mikulski
The Honorable Frank R. Lautenberg
The Honorable Jack Reed
United States Senate

Managing the risk of exposure to pesticides is important for all Americans, but especially for children, whose developing systems can be more susceptible to harm. The Food Quality Protection Act of 1996 (FQPA) requires the Environmental Protection Agency (EPA), which regulates the use of pesticides at the federal level, to reevaluate the amounts of pesticide residues allowed on or in food—known as tolerances. EPA must ensure that the tolerances are safe, that is, that there is a reasonable certainty that no harm will result from exposure from all food and nonfood sources. In doing so, unless another safety factor is determined to be appropriate, EPA is required to apply an additional 10-fold safety factor in setting tolerances to ensure the safety of foods for children. EPA is also required to ensure that there is reasonable certainty that no harm will result to children specifically from aggregate exposure to a pesticide from all sources (such as lawn treatments, household uses, and drinking water, as well as food). In addition, EPA must consider available information concerning the combined or cumulative effects on children from groups of pesticides that may act on the body in similar harmful ways. The law requires EPA to consider all these factors in reassessing tolerances for pesticide residues in foods, and in doing so, EPA must give priority to pesticides that appear to pose the greatest risk to public health.

You asked us to examine how EPA is applying these requirements of the FQPA. We focused our efforts on three questions:

- What approach has EPA developed for making decisions about applying the new safety factor?
- What progress has been made in considering aggregate exposure and cumulative effects?
- What progress has been made in reassessing tolerances for pesticide residues?

This report is based in part on a review of documents related to safety factor determinations and pesticide risk assessments, as well as a review of EPA's database for tracking tolerance reassessments. We supplemented this analysis with interviews at EPA, as well as with federal health agencies, chemical industry and environmental groups, and outside experts. We did not evaluate EPA's regulatory decisions or the quality of the data behind them. Appendix I provides further details on our methodology. We performed our work from October 1999 through July 2000 in accordance with generally accepted government auditing standards.

Results in Brief

When FQPA became law in 1996, EPA immediately began efforts to consider the additional safety factor for children, using available methods and data in an interim approach that has evolved over time. An internal committee now recommends whether to apply the additional safety factor in pesticide reviews, based on data completeness and evidence of increased susceptibility in children. Using this approach, EPA has made decisions about applying the additional safety factor for 105 of the more than 450 pesticides to be reassessed. It determined that an additional safety factor was necessary in 49 cases and not necessary in the remaining 56 cases.

EPA also has interim procedures in place for considering aggregate exposure, which incorporate available data on exposures from food, drinking water, and residential uses. Data on nonfood exposures have been lacking for most pesticides, however, and methods for estimating and combining such exposures are still being developed. EPA has not yet begun to consider cumulative effects in the regulatory process. It has determined that one group of pesticides that is considered to be high-risk, called the organophosphates, will need to be assessed for cumulative effects, but methods for doing so are still under development. The potential effects of considering aggregate exposure and cumulative effects are beginning to emerge. On June 8, 2000, after applying the additional safety factor and conducting an aggregate exposure assessment for chlorpyrifos (an organophosphate sold as Dursban, and the most widely used household pesticide in the United States), EPA announced a need to substantially reduce children's exposure to this pesticide by reducing its use on foods frequently eaten by children and by eliminating nearly all household uses. EPA has not completed aggregate exposure reviews for all 39 organophosphates individually, but when it does, a cumulative assessment will be required for the group, which may identify the need for additional changes.

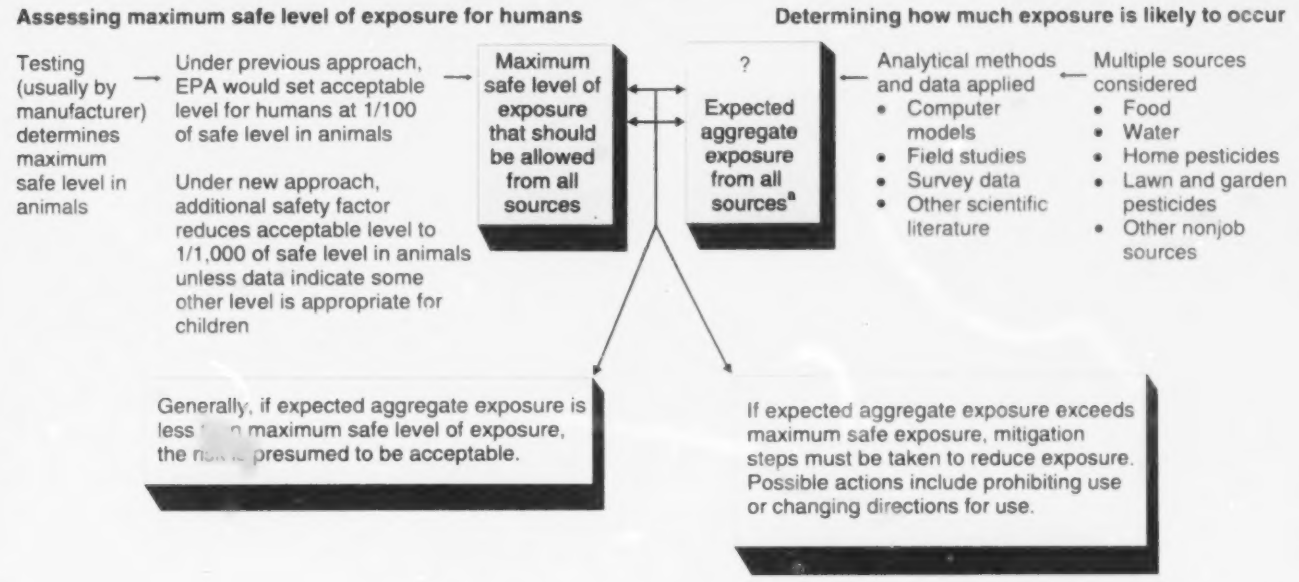
EPA has reported progress in reassessing existing tolerances for pesticide residues on foods, but relatively few of these allowable limits have changed as a result of considering FQPA's new requirements. The act called for reassessing one-third of all existing tolerances by August 1999—a goal EPA met. We analyzed a somewhat larger group, those counted as reassessed through April 2000. For about 47 percent of these tolerances, the manufacturer agreed with EPA to eliminate the tolerances and withdraw the pesticides from those uses (a pesticide has a separate tolerance for each food crop it is used on), before the additional safety factor or aggregate exposures were considered. In most of these cases the pesticide was no longer being used on a particular food crop or the manufacturer decided not to maintain the ability to use it on a particular food crop. Most of the remaining reassessments in the group we analyzed resulted in no change. In reassessing tolerances, EPA has given priority to high-risk chemicals. Some high-risk pesticides have been reassessed. However, the only tolerances counted as reassessed for the high-risk organophosphate pesticides were ones that were canceled voluntarily, because the organophosphates will require a cumulative assessment before existing tolerances can be formally reassessed.

Background

In essence, evaluating and managing the risk from exposure to pesticides involve determining the maximum safe level of exposure to a pesticide and assessing whether expected actual exposure is below this maximum level.[1] Figure 1 shows how these two steps relate to each other. As long as the expected exposure remains lower than the maximum safe exposure, the risk created by use of the particular pesticide is within acceptable limits and usually no action is required. However, once expected actual exposure levels exceed the maximum safe amount, EPA must determine the best ways to reduce exposure below the safe level to mitigate the risk. Many possible risk mitigation actions may be applied, ranging from prohibiting an agricultural or residential use of the pesticide to changing directions for its use (such as spraying less often). These mitigation steps are intended to reduce overall exposure from all sources, including exposure through pesticide residues on foods.

[1]The word "pesticide" is used broadly here to include insecticides, herbicides, fungicides, rodenticides, and the like, which are designed to prevent, destroy, repel, or reduce pests.

Figure 1: Overview of Risk Assessment and Mitigation for Pesticide Exposure


Assessing maximum safe level of exposure for humans
Determining how much exposure is likely to occur
Testing (usually by manufacturer) determines maximum safe level in animals
Under previous approach, EPA would set acceptable level for humans at 1/100 of safe level in animals
Under new approach, additional safety factor reduces acceptable level to 1/1,000 of safe level in animals unless data indicate some other level is appropriate for children
Maximum safe level of exposure that should be allowed from all sources
?
Expected aggregate exposure from all sources[a]
Analytical methods and data applied
• Computer models
• Field studies
• Survey data
• Other scientific literature
Multiple sources considered
• Food
• Water
• Home pesticides
• Lawn and garden pesticides
• Other nonjob sources
Generally, if expected aggregate exposure is less than maximum safe level of exposure, the risk is presumed to be acceptable.
If expected aggregate exposure exceeds maximum safe exposure, mitigation steps must be taken to reduce exposure. Possible actions include prohibiting use or changing directions for use.

[a]If this pesticide is part of a group that acts on the body in similar harmful ways, EPA must assess risk based on cumulative effects, that is, the combined aggregate exposure for each pesticide in the group.

New Law Fundamentally Changed How Risks Are Assessed

FQPA made several fundamental changes in how EPA assesses and manages pesticide exposure risks to humans.[2] Under FQPA, EPA must reevaluate existing tolerances for pesticide residues in foods within 10 years. In doing so, EPA is required to (1) apply an additional 10-fold safety factor in setting tolerances to ensure the safety of foods for children, unless reliable data support a different factor; (2) ensure that there is reasonable certainty that no harm will result to children from aggregate exposure to a pesticide from food, drinking water, and residential sources; and (3) consider available information concerning the cumulative effects on children of pesticides that act in a similar harmful way (known as a common mechanism of toxicity). These FQPA requirements also apply in

[2]FQPA amended existing laws that are intended to protect the public from harmful exposures to pesticides. The amended laws were primarily the Federal Insecticide, Fungicide, and Rodenticide Act (7 U.S.C. 136 et seq.) and the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 301 et seq.).

setting tolerances for new pesticides that are being registered and for new uses of existing pesticides. In reassessing existing tolerances, EPA must give priority to pesticides that appear to pose the greatest risk to public health. Table 1 provides a brief overview of these requirements.

Table 1: Key Pesticide Regulatory Requirements Added by FQPA

Requirement	Explanation
Applying an additional safety factor for children	To account for differences in sensitivity between humans and test animals, as well as differences in sensitivity among different people, EPA routinely applies a safety factor for humans that sets the maximum acceptable or safe level of exposure to a pesticide at 1/100 of the maximum amount observed as safe in animals. The additional safety factor for children generally reduces the safe level by another factor of 10, thereby lowering it to 1/1,000 of the amount for animals.
Considering aggregate exposure	Aggregate exposure is the exposure to a single pesticide that a person would be likely to face from all sources, including food, drinking water, and home and garden use of the pesticide. Before FQPA, EPA was required only to assess exposure from food, although in practice the agency sometimes considered other sources as well.
Considering cumulative effects	The cumulative effects of exposure are those that a person would be likely to face from the combined aggregate exposures to several pesticides that act on the body in similar harmful ways. Groups or classes of pesticides that act in a similar way are said to have a common mode of action or a common mechanism of toxicity. When EPA determines that a group of pesticides has a common mechanism of toxicity, it must consider the aggregate exposure from every pesticide in the group.
Reassessing tolerances	A tolerance is the maximum legal amount of a pesticide residue that is allowed to remain on a food commodity that has been treated with the pesticide. It is usually expressed in parts per million or parts per billion. The allowed residue from the use of one pesticide on one specific crop, such as apples or asparagus, represents one tolerance. Thus a single pesticide may have many tolerances. FQPA requires EPA to reassess all tolerances in effect prior to passage of the law in August 1996 (9,721 tolerances for more than 450 pesticides) to ensure that they are safe for children.

Among the difficulties EPA has faced in implementing FQPA requirements is the fact that the scientific knowledge necessary to accomplish some of these new mandates did not exist in 1996. EPA's pesticide regulatory process has traditionally focused on exposures from food and considered each pesticide separately. Under FQPA the agency has been required to develop the methods and data to perform the new aggregate exposure and cumulative effects assessments, which incorporate exposures from

nonfood sources and the combined effects of entire classes of pesticides that were previously considered individually.

The first class of pesticides to be affected by cumulative assessment under FQPA will likely be the organophosphates. EPA has identified the organophosphates as a class of pesticides requiring cumulative assessment because they can impair nervous system function by inhibiting the enzyme cholinesterase. The organophosphates are older pesticides, and EPA considers some of them to be more hazardous (although not all older pesticides are necessarily more hazardous). They are of special concern because of their toxicity and widespread use both in agriculture and in homes and gardens, according to the National Research Council's 1993 report, *Pesticides in the Diets of Infants and Children*.[3] One of them is the single most widely used household pesticide in the United States—chlorpyrifos, which is sold under such names as Dursban and Lorsban.

EPA's Office of Pesticide Programs Has Main Responsibility for Implementation

EPA's Office of Pesticide Programs (OPP) has the lead responsibility for implementing the new FQPA requirements within its existing system of pesticide regulation. This system includes registering or licensing new pesticide products for use in the United States and reevaluating older pesticides to ensure that they meet current health standards and that their risks are adequately mitigated (a process required to reregister the pesticide for continued use).[4] Nearly 900 people organized into nine OPP divisions carry out these activities. Two divisions have the main responsibility for managing pesticide risk assessments: the Registration Division (for assessing new chemicals and new uses of existing chemicals) and the Special Review and Reregistration Division (for assessing most

[3]National Research Council, *Pesticides in the Diets of Infants and Children* (Washington, D.C.: National Academy Press, 1993), pp. 17, 245-46.

[4]As directed by the 1988 amendments to the Federal Insecticide, Fungicide, and Rodenticide Act, EPA has been conducting a comprehensive review of pesticides initially registered before November 1, 1984, to determine their eligibility for reregistration.

conventional chemical pesticides for reregistration and for reassessing tolerances as required by FQPA).[5]

To help conduct these risk assessments, the two divisions use analyses provided primarily by another division, the Health Effects Division. Scientists in the division examine the substantial body of studies and data reports that under regulation are required to be submitted by the pesticide's registrant (that is, the applicant for registration, usually the manufacturer), along with other available data, to ensure the reliability of the studies, assess the toxicity of the pesticide under review, and estimate the risks of exposure. Sources of possible exposure that are considered include water and residential contamination, in addition to the traditional focus on food exposures. The risk assessments are subject to internal peer review by the Health Effects Division staff.

Approach for Making Safety Factor Decisions Continues to Evolve

Soon after FQPA became law in 1996, EPA began to include consideration of the additional safety factor for children in its pesticide risk assessments, as required. EPA developed interim guidelines for determining whether this additional safety factor should be applied, and these procedures have evolved over time.[6] Under this approach, an internal review committee of scientists, managers, and other experts within OPP—the FQPA Safety Factor Committee—takes lead responsibility for recommending whether the additional safety factor should be applied, with OPP management making the final decisions. By March 2000, this committee had reviewed and prepared safety factor recommendations for 150 pesticides, and OPP management had made final safety factor decisions for 105 of them.

[5]While OPP regulates all types of pesticides, we focused our review on the largest group, the conventional pesticides, leaving aside antimicrobials and biopesticides. These other types of pesticides are the responsibility of OPP's Antimicrobial Division and Biopesticides and Pollution Prevention Division, respectively. Those two divisions both assess and manage the risks associated with chemicals under their purview. FQPA standards apply, and reassessed tolerances for antimicrobials and biopesticides are counted in the EPA Tolerance Reassessment Tracking System.

[6]EPA's interim guidelines are operating policies and procedures that the agency follows to make the decisions required by FQPA, such as whether to apply the additional safety factor for children, while the process of developing more complete, formal policies and procedures continues. Decisions made under interim guidelines may be revisited, if appropriate, as methods and data are improved and policies refined.

Approach for Considering Additional Safety Factor Has Evolved Since 1996

EPA began to consider the additional safety factor in its pesticide reviews and tolerance reassessments soon after FQPA was passed. By October 1996, EPA had drafted an initial version of its approach to applying the additional safety factor, and by January 1997 it had issued a notice providing detailed guidelines for manufacturers on how pesticide reviews for registration and reregistration would proceed, taking the new FQPA requirements into account.[7] In March 1997, EPA published an implementation plan for FQPA that addressed how it would consider the additional safety factor for children. The implementation plan called for applying the following approach:

- EPA would require the additional 10-fold safety factor for children if the agency lacked complete and reliable data to assess pre- or postnatal toxicity relating to infants and children or if the data indicated pre- or postnatal effects of concern.
- If data were incomplete, an additional safety factor between 3 and 10 would be applied, with the size of the factor depending on how much information was incomplete and the seriousness of any concerns about effects.
- If data were sufficient to demonstrate no potential pre- or postnatal effects of concern, no additional safety factor would be applied.

To make recommendations to OPP management about applying the safety factor in individual pesticide risk assessments, OPP established a Safety Factor Committee in February 1998.[8] This internal peer review group is composed of risk assessors (including toxicologists and exposure experts) from OPP science divisions and risk managers (staff responsible for risk mitigation activities) from the divisions that regulate most of the

[7]Pesticide Registration Notice 97-1 stated that data requirements for pesticide registrations and reregistrations would not be revised immediately to reflect the new FQPA requirements. The notice included, however, a detailed outline of the additional data and studies that EPA was requesting from registrants on a voluntary basis to support timely pesticide reviews under FQPA.

[8]EPA officials told us that, up to that time, two predecessor groups had conducted the reviews. The first was the Reference Dose Committee in the Health Effects Division, which was responsible for reviewing pesticide toxicity data at the time FQPA was passed. It continued its reviews, including consideration of the new safety factor, until summer 1997, when a new group was established for that purpose. This second group was the Hazard Identification Assessment Review Committee, a committee that still reviews the toxicology database for each pesticide to determine what adverse health effects the pesticide might cause. This committee performed a limited number of reviews, based on toxicity data only.

chemicals. The committee's procedures call for systematically reviewing both toxicology and exposure data for each chemical, focusing on two overriding concerns: (1) uncertainties in the data used for the toxicology and exposure assessments (data gaps) and (2) evidence of increased susceptibilities in infants and children (the potential for pre- and postnatal toxicity).[9] Examples of the types of questions considered in these subject areas are presented in table 2.

Table 2: Examples of Questions Considered in Safety Factor Reviews

Subject area	Questions
Toxicology	Do we have adequate hazard (toxicity) studies to evaluate risk to infants and children? Do these studies show enhanced susceptibility in infants and children? That is, do the effects in the young occur at doses that do not cause effects in adults?
Food exposure	What kinds of residue databases are available for each crop (for example, field study data or monitoring data) and what are their sources? Is information available on percentage of crop treated? According to food consumption data, which crops contribute significantly to the diet for adults? For infants and children?
Drinking water exposure	Are models or monitoring data used to estimate drinking water exposure? If models are used, what scenarios are used in the model, and what are the resulting estimated environmental concentrations? If monitoring data are used, what kinds of data were collected and under what conditions (for example, from vulnerable areas at maximum label rates)?
Residential exposure	Is the compound used around the home in such a way that children and infants may be exposed? What are the frequency and rate of application? Are reliable biologically based exposure data or epidemiology data available to support the results of the assessment (for example, incident reports or Centers for Disease Control and Prevention biomonitoring data)?

Committee members are encouraged to apply scientific judgment as well as qualitative and quantitative data in reaching consensus on whether to apply, reduce, or remove the safety factor. The committee considers

[9]According to an EPA official, the data studies that are most useful in assessing pre- and postnatal toxicity are the prenatal developmental toxicity studies in rats and rabbits, the two-generation reproductive toxicity study in rats, and, when available, the developmental neurotoxicity study in rats. All of these studies are done using pregnant and young animals. The first two studies are always required for assessing food use pesticides, and the third study (the developmental neurotoxicity study) is conditionally required.

written reports and oral presentations and seeks to reach a consensus in each case on the FQPA safety factor it will recommend to OPP managers.[10]

As of March 2000 the committee had reviewed 150 pesticides and submitted safety factor recommendations to OPP managers. In reviewing the committee's justifications for its recommendations, we found that when the committee identified both toxicology data gaps and evidence of increased susceptibility in children, the pesticides were most likely to receive a recommendation for a 10-fold safety factor. When there was no evidence of increased susceptibility, but incomplete data, a safety factor was also recommended, but it was less than 10 when the data suggested that a lower safety factor was sufficient. Pesticides with neither increased susceptibility nor data gaps usually received a recommendation for no additional safety factor.

While EPA has incorporated consideration of the new safety factor in its pesticide reviews, it has continued efforts to refine its policies on applying the safety factor. A formal policy document on the safety factor has been developed (it is not a regulation), which discusses in detail the legal framework, overall approach, and related toxicology and exposure issues. It is much more extensive than the guidelines under which the Safety Factor Committee has been operating, but is consistent with them. An EPA official explained that the two documents serve somewhat different purposes, with the policy document providing comprehensive discussion of the issues and the operating procedures translating those policies into practical guidelines. The safety factor policy document was released for public comment in 1999. As of July 2000, an agency official told us that EPA was still assessing the comments it had received, and the document had not yet been issued in final form.

No Additional Safety Factor Has Been Applied in Half of Decisions

OPP senior managers make the final decisions about whether to apply the additional safety factor for children, based on the Safety Factor Committee's recommendations and other considerations. As of the end of March 2000, OPP had made safety factor decisions for 105 of the 150 pesticides the Safety Factor Committee had reviewed. OPP determined that a safety factor to protect children, in addition to the routinely applied

[10]In the few cases in which the committee could not reach a consensus recommendation, a memorandum was prepared to division directors for their decision. An example of this situation is dicofol, a pesticide case described in app. II.

100-fold safety factor, was necessary in 49 cases and that available evidence was sufficient to show that an additional safety factor was not required in 56 cases (see table 3). For the organophosphate pesticides, OPP decided to apply the additional safety factor in 24 cases and not to apply it in 15.

Table 3: Safety Factor Decisions

		OPP decision			
Type of pesticide	**Number reviewed**	**No additional factor**	**3-fold factor**	**10-fold factor**	**Factor greater than 10-fold**
Organophosphates	39	15	12	10	2
All others	66	41	11	11	3
Total	**105**	**56**	**23**	**21**	**5**
Percentage of total		53%	22%	20%	5%

In most cases, OPP managers adopted the committee's recommendations for the level of safety factor to protect children, but in some cases they increased those levels. In 19 of the 105 decisions, the factor was increased (made more protective) to account for other types of uncertainties. OPP officials said these uncertainties most often related to serious data gaps or special concerns about the severity of a pesticide's health effects. In 5 cases, OPP increased the combined safety and uncertainty factors to greater than 10-fold.[11]

To provide an indication of whether EPA was following its procedures, we selected three high-risk pesticides of different types (including one organophosphate) that had gone through the safety factor review process and asked a consultant with expertise in environmental toxicology to review the process and results. These three examples are described in appendix II. The consultant concluded that in all three cases EPA's actions were thorough and its conclusions reasonable.

[11]OPP most often applied a higher safety factor when a risk assessment used a "lowest-observed-adverse-effect level" in animal studies as a threshold no-harm level, instead of the preferred "no-observed-adverse-effect level," and thus was less certain and protective. Safety factors for one pesticide, for example, were increased by the FQPA 10-fold factor for children and multiplied by an additional 10-fold factor for uncertainties.

Procedures Are in Place for Considering Aggregate Exposure but Not Cumulative Effects

EPA has interim procedures in place for considering aggregate exposure in its pesticide reviews and tolerance reassessments. These procedures incorporate available data on exposures from drinking water and residential uses, along with food exposures. Efforts are being made to improve available data on nonfood exposures and the methods for estimating combined exposures to individual pesticides from all sources. Efforts to consider the cumulative effects of exposure to groups of similar pesticides have not progressed as far as those for aggregate exposure. EPA has adopted policies for identifying classes of pesticides that have a common mechanism of toxicity, but methods for conducting cumulative assessments for these classes of pesticides are still under development. As a result, EPA has not yet considered cumulative effects in its pesticide risk assessments. In the case of the organophosphates—and chlorpyrifos in particular—the potential effects of aggregate exposure and cumulative assessments, in terms of needed mitigation steps, are beginning to emerge.

Interim Procedures for Aggregate Exposure Assessments Are in Place

Although formal policy guidance for performing aggregate exposure assessments has not yet been issued in final form, EPA has interim procedures in place for considering aggregate exposure using available data and methods.[12] Traditionally, EPA has assessed the risk of food use pesticides on the basis of estimated exposure from all foods containing residues of the pesticide. Under FQPA, EPA must also take into account the amount of exposure to each pesticide that is likely to occur from drinking water and from uses in and around the home. Common residential uses include lawn and gardening uses, pet applications, and roach and termite treatments. Not all pesticides have residential uses, but for those that do, adding those types of exposures to food and water exposures might push the total beyond the maximum safe level of exposure, leading to a need for mitigation steps and possible changes in tolerances.[13]

Because of its traditional focus on pesticide exposures from foods, EPA's data and methods for estimating food exposures are relatively highly developed, but for most pesticides the agency has lacked the data and

[12]The latest draft of the policy guidance for performing aggregate exposure assessments, dated October 1999, was being revised to respond to public comments for release in summer 2000.

[13]In app. II, phosmet provides an example of a pesticide with residential uses of concern, in this case as an insecticide for home and garden use and a flea dip treatment for dogs.

methods to estimate nonfood exposures from drinking water and residential uses. Moreover, EPA has lacked a method for combining exposures from these sources to estimate aggregate exposure. While such data and methods are being developed, the agency is using an interim approach that relies on available data and conservative scientific judgments to protect health; that is, in most cases the high-end estimates for drinking water and residential exposures are added to the estimated food exposure.

Estimating exposures from pesticides used in and around the home has been a particular challenge for EPA. In a working paper on assessing these residential exposures, EPA stated that it relies primarily on the scientific literature and industry sources because it lacks data for most pesticides to characterize exposures from nonfood sources. Many types of needed data still are not available. For example, an official told us that results from an effort initiated in 1995 to collect data on outdoor residential exposures (mainly from lawn chemicals) are only now coming in, and other efforts to collect data on indoor residential exposures and commercial pesticide applications are still under way. Methods for using such data to estimate residential exposures are being developed, which, when approved by EPA's Scientific Advisory Panel, will apply to both aggregate exposure and cumulative assessments. EPA intends that ongoing development and refinement will follow, as the agency gains experience with the methods.

Development of Methods to Assess Cumulative Effects Is Under Way

Developing ways to assess both aggregate exposure and cumulative effects has been more difficult and time-consuming than EPA anticipated, but developing approaches to cumulative effects assessment has proved particularly difficult. Experts in toxicology, exposure assessment, and risk assessment methodologies have indicated that the science necessary to successfully factor in these types of exposures, especially for cumulative effects, is a work in progress. Beginning in 1997, EPA contracted with the International Life Sciences Institute (ILSI)[14] to convene workshops that EPA hoped would bring together representatives of industry and academia and other interested parties to participate in developing the new exposure assessment policies required under FQPA. An ILSI group worked on

[14]ILSI is a nonprofit worldwide foundation established in 1978 to advance the understanding of scientific issues relating to nutrition, food safety, toxicology, risk assessment, and the environment. Its Risk Science Institute, established in 1985, seeks to advance and improve the scientific basis of risk assessment.

aggregate exposure assessment methods in 1997 and 1998, and another workshop reported on a framework for cumulative risk assessment in 1999.

Because of the complexity of the scientific issues involved, EPA has included considerable review by experts both inside EPA (including staff and advisory committees) and in the academic and research communities in its development of ways to measure aggregate exposure and cumulative effects. According to one EPA official, while this peer review likely provided benefits, it also slowed the process. The review has come from such groups as EPA's Scientific Advisory Panel and the Tolerance Reassessment Advisory Committee, which also have provided review of policies related to other aspects of implementing FQPA.[15] The Scientific Advisory Panel, which has been the main source of ongoing peer review, now meets about every 2 months for 4 to 5 days, the official told us. All panel meetings are open to the public, industry, and environmental groups. Obtaining review from the Tolerance Reassessment Advisory Committee required substantial time and resources, according to the official, because many background and policy documents had to be prepared.

To put cumulative assessment in place, EPA first needed methods to identify groups of pesticides that act on the body in similar ways to cause adverse health effects. A January 1999 document laid out the principles EPA applies to determine if a group of pesticides acts through a common mechanism of toxicity. Using these principles, EPA has identified the organophosphates as one such group of pesticides because they impairnervous system function by inhibiting the enzyme cholinesterase.[16] The next step, developing the methods for actually conducting cumulative assessments, has been more difficult and time-consuming, and the first

[15]The Scientific Advisory Panel is a scientific peer review group that advises EPA on major issues. It has reviewed and commented on science policy issues and their related guidance documents, including the policies and procedures for applying the safety factor and methods for aggregate exposure and cumulative assessments. Panel members are mainly from academia or other government agencies. The Tolerance Reassessment Advisory Committee met from May 1998 through October 1999. It included representatives of the pesticide industry, agricultural interests, and environmental groups who were convened by EPA to identify key science policy issues affecting risk assessment. It was replaced by a new group, the Committee to Advise on Reassessment and Transition, in June 2000.

[16]According to an EPA official, OPP has identified two other groups of pesticides that have a common mechanism of toxicity and are candidates for cumulative risk assessment: the cholinesterase-inhibiting carbamates and some of the chloroacetanilides.

draft of the methodology was not released for public comment until June 2000.[17]

EPA has not yet conducted a cumulative assessment. In addition to the need for an acceptable methodology, a cumulative assessment requires aggregate exposure assessments for each of the individual pesticides in the cumulative effects group. While aggregate exposure assessments are in process for the 39 organophosphates, they are not all complete. Nonetheless, EPA agency staff expect to present a pilot test of the proposed cumulative assessment methodology to the Scientific Advisory Panel in September 2000, using a case study of 25 organophosphate pesticides (including 7 chemicals with residential uses and 2 with water residues). The pesticides will not be named, to encourage focus on the assessment process, but the data will be real and fairly complete.

Potential Effects of Aggregate Exposure and Cumulative Assessments Beginning to Emerge

EPA currently lacks the methods to consider cumulative effects associated with classes of pesticides that have a common mechanism of toxicity, such as the organophosphates, but the potential effects of aggregate exposure assessment can be seen in the example of chlorpyrifos (sold under such names as Dursban and Lorsban), a major organophosphate pesticide that has many food and residential uses. Chlorpyrifos is found in many insect sprays and is the single most widely used household pesticide in the United States. It is also used by many commercial growers. In this instance, EPA has applied an additional 10-fold safety factor to protect children and has assembled considerable data about aggregate risk from the many sources of possible exposure to chlorpyrifos. At a technical briefing on June 8, 2000, EPA announced agreement with the pesticide's manufacturer to eliminate all home, lawn, and garden uses of the pesticide, to eliminate the majority of termite control uses, and to significantly lower allowable pesticide residues on several foods regularly eaten by children, such as apples, grapes, and tomatoes. These mitigation steps are intended to reduce expected aggregate exposure below the maximum safe level.

Whether actions similar to those for chlorpyrifos will result from considering aggregate exposures to other less widely used organophosphate pesticides is unknown. However, when EPA conducts a cumulative assessment, combining aggregate exposures for all the

[17]The draft was released for public comment on June 29, 2000. Following the comment period, EPA plans to revise the draft and publish it in final form, but no date has been set.

pesticides in this group, additional mitigation steps may be necessary to protect children's health.

EPA Has Made Some Progress in Reassessing Tolerances to Date

EPA has made some progress in reassessing existing tolerances, as required by FQPA, but relatively few of these allowable limits for pesticide residues have changed as a result of considering the law's new requirements. As of April 2000, EPA reported that it had reassessed nearly 3,500 tolerances for about 300 pesticides.[18] However, nearly half of these tolerance reassessments did not require consideration of the additional safety factor for children or aggregate exposure, because the manufacturer agreed with EPA to voluntarily eliminate the tolerances and withdraw the pesticides from those uses. Most of the other reassessed tolerances were unchanged. Although EPA has given priority to reassessing tolerances for high-risk pesticides, reassessments for the high-risk organophosphate pesticides cannot be completed until a cumulative assessment has been done for the group.

EPA Reports That Nearly 3,500 Tolerances Have Been Reassessed

FQPA requires EPA to reassess all food use tolerances that were in effect prior to passage of the law in August 1996—9,721 tolerances—to ensure that the maximum residue levels they allow reflect any changes that might result from the act's new protections. EPA must complete these tolerance reassessments within 10 years of FQPA's enactment on a specific schedule: one-third by August 1999, two-thirds by August 2002, and the rest by August 2006.

According to EPA, 3,290 tolerances (34 percent of the total) had been reassessed by August 1999, the date of its first deadline. EPA also announced that 2,178 (66 percent) of those reassessed tolerances were for pesticides in the highest risk group. By April 2000, when we conducted our analysis, the number of tolerance reassessments stood at 3,471, or 36 percent of the total.

[18]EPA sets a tolerance for each use of a pesticide on a single food product; thus pesticides applied to many types of food will have multiple tolerances. Some pesticides have more than 100 tolerances.

Nearly Half of Tolerances Were Eliminated Voluntarily

Our analysis of the 3,471 tolerances that EPA counted as reassessed in April 2000 showed that nearly half of them—1,638 tolerances, or 47 percent—did not involve consideration of the new FQPA requirements. Most of these (1,257) were eliminated or canceled by EPA, with the manufacturer's agreement, before risk assessments for the associated pesticides were completed.[19] Tolerance reassessments considered to be voluntary removals or cancellations generally fell into two categories:

- Tolerance no longer needed. When a particular use (for example, on apples) has been removed from the list of registered uses for a pesticide, a tolerance is no longer needed for that use. There were cases in which tolerances for previously removed uses had not yet been canceled, and if they were not needed for imported foods, EPA completed the cancellation process.[20]
- Manufacturer withdraws support. Manufacturers may withdraw support for certain tolerances for a variety of reasons. For example, they may determine that the costs of continued registration of the pesticide for that use—including the costs of additional testing and registration fees—are not justified by market conditions. An EPA official told us that in a number of these cases, risk concerns that the agency expressed about the associated pesticide contributed to the manufacturer's decision to drop the tolerance.

Most Tolerance Reassessments That Considered FQPA Requirements Were Unchanged

Fifty-three percent of the tolerance reassessments (1,833) were based on pesticide risk assessments that considered aggregate exposure and the additional safety factor for children. Most of these tolerance reassessments—1,421 tolerances, or 77.5 percent—resulted in no change (see table 4). The remainder of the tolerances were revoked (eliminating the use), lowered (allowing less residue), or raised (allowing more residue).

[19]The remainder of the tolerances that were canceled in this way involved biological pesticides regulated by another EPA division, inert ingredients and some other pesticides exempted from FPQA's requirements (for example, for not applying to food, such as use on tobacco), and other special circumstances.

[20]An import tolerance is maintained for imported foods for which there is no U.S. registration for the pesticide in question. FQPA applies the same standards to imports as it does to other tolerances.

Table 4: Results of Tolerance Reassessments Involving FQPA Considerations

		Tolerance decision			
	Total reassessed	Kept same	Revoked	Lowered (allows less residue)	Raised (allows more residue)
Number	1,833	1,421	98	139	175
Percentage		77.5%	5%	8%	9.5%

EPA officials indicated that only a small percentage of tolerances were lowered, even after the additional safety factor and aggregate exposures were considered, because historically the agency has set tolerances conservatively. As a result, they said, many tolerances were already at levels that would pass FQPA's more stringent requirements. Likewise, EPA officials told us that their decisions to raise 175 tolerances (that is, to allow an increased concentration of pesticide residue to remain on the food) do not represent an unacceptable risk to children or the general population. Instead, the raised tolerances reflect new data from additional studies or field trials that allowed EPA to perform more refined analyses of pesticide exposure and risk.

Tolerance Reassessments for High-Risk Organophosphates Have Not Been Completed

FQPA required EPA to give priority to reassessing tolerances for high-risk chemicals, and in August 1997 the agency published a *Federal Register* notice[21] that divided the pesticides with tolerances requiring reassessment into three priority groups by level of risk. The highest priority group, Group 1, which EPA considers to be the highest risk, included the organophosphates, probable cancer-causing chemicals, and other pesticides of particular concern. This group accounts for the largest proportion, about 57 percent, of all tolerances that need to be reassessed.[22]

[21] *Federal Register*, vol. 62, no. 149, pp. 42020-30, Aug. 4, 1997.

[22] Group 1 (228 pesticides/5,546 tolerances), the highest-risk chemicals, includes the organophosphates, carbamates, organochlorines, and probable carcinogens. Group 2 (93 pesticides/1,928 tolerances) includes the lower-risk possible carcinogens and all remaining reregistration chemicals (those that were first registered before 1984). Group 3 (148 pesticides/2,247 tolerances) includes the remaining pre-FQPA pesticides with reregistration eligibility decisions, the remaining post-1984 pesticides, biological pesticides, and the remaining inerts.

Of the 3,471 tolerances that EPA has counted as reassessed through April 2000, two-thirds (2,286, or 66 percent) were for pesticides in Group 1. This represents reassessment of 41 percent of all tolerances for the high-risk pesticides. Less than 30 percent (483 of 1,691) of tolerances for the high-risk organophosphate pesticides were counted as reassessed, and most of these were canceled voluntarily. Even though safety factor decisions have been made for 39 organophosphates and risk assessments including aggregate exposure are in process, EPA has been unable to finalize the pesticide risk assessments and their associated tolerance reassessments, because the individual reviews must be combined in a cumulative assessment for all of the organophosphates.

Conclusions

FQPA brought substantial changes to EPA's pesticide regulatory process, and these changes are still works in progress. Some of the tools needed by EPA to implement FQPA were not available when the law was enacted. EPA set about developing the necessary procedures, methodologies, and data almost immediately. The agency has adopted a series of interim approaches while specifying, with the assistance of peer reviewers, more refined permanent methods, which are now nearing completion. EPA has made progress in reviewing pesticides and reassessing tolerances since 1996, but so far relatively few tolerances have changed as a result of considering the new FQPA requirements. While it is too early to tell what the future effects of FQPA may be, the next few years could bring substantial changes, as the organophosphates and other groups of high-risk pesticides are reconsidered in the light of their aggregate exposures and cumulative effects. It appears that EPA's recent decision on chlorpyrifos, for example, will result in major changes in the uses of that pesticide that are intended to protect people, and children in particular, from potentially adverse health effects.

Agency Comments

We provided a draft of this report for comment to EPA, which supplied technical comments that we incorporated where appropriate.

We will send copies of this report to the Honorable Carol Browner, EPA Administrator, appropriate congressional committees, and other interested parties. We will also make copies available to others on request.

If you or your staffs have any questions about this report, please call me at (202) 512-7119. Major contributors to this report are listed in appendix III.

Janet Heinrich

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Associate Director, Health Financing
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Methodology

To examine how EPA is making decisions about applying the new safety factor for children, we obtained documentation for each FQPA safety factor determination. This consisted of three documents: (1) a summary log of recommendations made by the Safety Factor Committee as of March 21, 2000, with justifications for these recommendations, (2) a list of final decisions made by OPP managers for regulatory purposes, and (3) a "Safety Factor Report" dated March 22, 2000, which explains the differences between the Safety Factor Committee recommendations and the final safety factor decisions. We synthesized information from these lists with other documentary evidence obtained from EPA, as well as information from EPA's Tolerance Reassessment Tracking System (discussed below), to summarize the results of FQPA safety factor decisions made to date. In addition, we obtained detailed documentation and support material for three pesticides that were reviewed by the Safety Factor Committee and asked a consultant with expertise in environmental toxicology, H.B. Matthews, Ph.D., Society of Toxicology Congressional Fellow, to review those cases in depth. We did this to provide specific examples of EPA processes and their results and to determine whether EPA's processes for assigning FQPA safety factors seemed reasonable.

To determine what progress EPA has made in considering aggregate exposure and cumulative effects, we obtained documents showing the development of policies and procedures, including numerous interim drafts, and interviewed EPA officials regarding the history behind the development of these policies. We also held numerous discussions with EPA officials to determine the extent to which EPA has assessed aggregate exposure and cumulative effects in the pesticides reviewed since passage of FQPA, and the schedule for the completion and implementation of the policies. Information on EPA's plans, schedule, and progress in reassessing the group of organophosphate pesticides is available on the OPP Web site at www.epa.gov/pesticides/op/status.htm.

Finally, to identify what progress has been made in reassessing tolerances, we obtained EPA's Tolerance Reassessment Tracking System database current to April 11, 2000. EPA created this database to track the agency's progress in meeting the deadlines associated with FQPA's requirement to reassess all tolerances. The tracking system contains extensive information on all permanent pesticide tolerances registered as of August 1996, as well as data on each pesticide associated with the tolerances. In order to examine the agency's use of the FQPA safety factor in assessing risk for each pesticide, we added to the database a field containing the specific safety factor decisions for each chemical. Because most pesticides in the

tracking system have more than one tolerance, we associated each pesticide's safety factor with all tolerances for that chemical.

We used the tracking system to identify groups of tolerances and pesticides with specific attributes by creating a series of database filters. For example, by selecting for tolerances EPA counted as reassessed, which had an FQPA safety factor decision, but were not reassessed administratively through notices in the *Federal Register*,[1] we identified those tolerances that were reassessed as the result of a complete pesticide risk assessment, including an FQPA safety factor decision and consideration of aggregate exposures. Similarly, we used various criteria to determine other attributes of the tolerances EPA has counted as reassessed, such as pesticide type (organophosphate, carbamate, organochlorine, and so on), risk priority group (Group 1, 2, or 3), and the resulting tolerance reassessment actions (raise, lower, same, or revoke).

[1]EPA officials told us that the tolerances counted as reassessed administratively through notices in the *Federal Register* were not the result of a full pesticide risk assessment and hence were not affected by an FQPA safety factor decision.

Three Pesticides Evaluated Under FQPA's New Requirements: Dicofol, Methomyl, and Phosmet

We asked a consultant with expertise in environmental toxicology, H.B. Matthews, Ph.D., Society of Toxicology Congressional Fellow, to help us review three pesticide cases to provide detailed examples of how OPP considers the new FQPA requirements in its pesticide risk assessments. In these examples, we focused primarily on the work of the FQPA Safety Factor Committee, but we considered other aspects of OPP's review and decision-making process as well.

We selected three pesticides for review, using the following criteria: the pesticides selected must have received a final safety factor decision; must have tolerances to be reassessed under FQPA; and must be high-risk Group 1 pesticides[1] of different types, including an organophosphate; preferably should have multiple uses (tolerances), including nonfood residential uses requiring aggregate exposure assessment; and must be likely to affect children through food and other exposures. The pesticides we selected were dicofol, an organochlorine; methomyl, a carbamate; and phosmet, an organophosphate.

We obtained documents to describe the OPP review process for these three pesticides from the OPP officials who manage the FQPA Safety Factor Committee. We provided these documents to our consultant for his review, which focused on such basic questions as the following:

- As an overall conclusion, based on the input reports and committee deliberations, does the Safety Factor Committee's recommended safety factor appear to be reasonable and reasonably well justified?
- Did the committee follow its own review criteria in a systematic way?
- Did the committee adequately justify its decisions on (1) data completeness and reliability (data gaps) and (2) evidence of increased susceptibility in children?
- How did the committee consider aggregate exposures?
- Was cumulative assessment addressed in any way?

Our expert reviewer prepared comments addressing these questions for each of the pesticide examples, and in some cases provided additional information and opinion based on his own knowledge and experience. Those comments have been combined with a description of the pesticide and a summary of its review history in the sections below.

[1]Group 1 pesticides are those identified by EPA as the highest risk and whose tolerances require priority reassessment under FQPA.

Dicofol

Description

Dicofol is an organochlorine pesticide in EPA's high-risk Group 1. It is used primarily on cotton, apples, and citrus crops and has nonresidential uses on lawns and ornamental shrubs (for example, it may be used by professional applicators on golf courses and landscaping, but it may not be used by homeowners). Dicofol was first registered as a pesticide in the United States in 1957. There are 50 current food use tolerances registered for dicofol, all of which have been reassessed under FQPA requirements.

FQPA Review History

Dicofol was reviewed at one of the first meetings of the FQPA Safety Factor Committee, on March 30, 1998. Information was excerpted from the pesticide's reregistration document, which was nearly "Toxicological Considerations for FQPA Safety Factor Selection."

The reregistration document's "FQPA considerations" section presented the following conclusions: (1) the data provided no indication of increased sensitivity in young animals, but (2) a developmental neurotoxicity study was required, but not available (a data gap), because dicofol is an organochlorine, is structurally related to DDT (which is neurotoxic), and is considered an endocrine disruptor. A safety factor of 3 was recommended. The main concern in terms of exposure was for occupational users. However, at that time there were two homeowner uses, and no data were available to assess residential exposure. Because of this lack of data, the reregistration document recommended that residential use of dicofol be discontinued. The document stated that EPA did not have the methods or the data to consider potential cumulative effects from dicofol and other members of the organochlorine class of pesticides.

The Safety Factor Committee reviewed the information from the reregistration document for dicofol in March 1998 but was unable to reach a consensus decision because it was concerned that its recommendation could set a precedent for other endocrine disruptors. After seeking guidance from OPP division directors, the committee recommended a 3-fold safety factor.

OPP managers accepted this recommendation, and the revised (July 2, 1998) and final (November 1998) dicofol reregistration documents issued by EPA included the 3-fold FQPA safety factor. Reasons given were as

follows: (1) aggregate exposure concerns were reduced because the two residential uses were dropped, (2) cumulative effects from dicofol and other organochlorines could not be considered, (3) strong concerns regarding occupational exposure remained, and (4) significant risk mitigation actions were required, including voluntary cancellation of some uses by the registrant. Eligibility for reregistration was contingent on the results of a dermal toxicity study and a dislodgeable foliar residue study (to be submitted).

Reviewer's Comments

Our reviewer noted that dicofol is an old pesticide, which is only moderately toxic and not extremely persistent in the environment, with no remaining residential uses. It raises concerns because of its structural relation to DDT. Having considered the documents described above, he reported that EPA's review of dicofol was thorough, although this was one of the first pesticides the Safety Factor Committee reviewed and its procedures were not as explicit as they later became. In the reviewer's judgment, data for dicofol appeared to be complete, with the only identified data gap being the need for a developmental neurotoxicity study; and the decision that there was no evidence of increased susceptibility in children was well justified. He concluded that EPA and the Safety Factor Committee responded appropriately to FQPA requirements to consider aggregate exposures for dicofol. EPA was not prepared to consider cumulative effects at that time. The reviewer noted that because pesticides related to dicofol have been removed from the market, cumulative effects from dicofol and other organochlorines would be effectively limited.

Methomyl

Description

Methomyl is a carbamate insecticide, also in EPA's high-risk Group 1. It has a wide variety of registered uses on field, vegetable, and orchard crops, turf farms, livestock quarters, and commercial premises and refuse containers. It was first registered in the United States in 1968. There are 80 current food use tolerances for methomyl but no homeowner residential uses. Ornamental and greenhouse uses were canceled voluntarily during the course of the pesticide's review in 1998. Tolerance reassessment under FQPA has been completed.

FQPA Review History

Methomyl was reviewed by the Safety Factor Committee on April 6, 1998. The committee received a report from the internal toxicology review committee (known as the Hazard Identification Assessment Review Committee), along with a document known as the "FQPA Responses," which was prepared to address the committee's specific questions in its standard operating procedures.

The toxicology review committee's report reviewed the toxicology database, including a new study submitted by the registrant (21-day dermal toxicity in rabbits). Data gaps were identified: acute and subchronic neurotoxicity studies were required but not available. Consequently, data on cholinesterase inhibition, behavioral effects, and nervous system effects by the pesticide were missing. The neurotoxicity studies were required because methomyl is a carbamate (a class of pesticides with known neurotoxic effects) and neurotoxic effects from methomyl were seen in dogs and rabbits. The requirement for a developmental neurotoxicity study was noted as "reserved," pending the results of the acute and subchronic studies.

The Safety Factor Committee decided to recommend a 3-fold safety factor for methomyl, based on (1) no indication of increased susceptibility in children and (2) data gaps—specifically, the lack of acute and subchronic neurotoxicity studies. The committee reviewed exposure data for food and drinking water, but not for residential exposures because there were no residential uses. Data quality was considered generally high, and realistic assumptions (conservative models) were used.

The final reregistration document for methomyl, dated December 1998, reflected the 3-fold FQPA safety factor decision. Because there were no homeowner uses, the aggregate exposure assessment did not consider residential exposures. However, because methomyl is produced when another pesticide, thiodicarb, degrades, the aggregate risk assessment considered methomyl residues from applications of both methomyl and thiodicarb. The document also states: "The Agency does not have, at this time, available data to determine whether methomyl has a common mechanism of toxicity with other substances or how to include this pesticide in a cumulative risk assessment. For the purposes of this assessment, therefore, the Agency has not assumed that methomyl has a common mechanism of toxicity with other substances."

Reviewer's Comments

On the basis of his review of the EPA documents, our reviewer felt that a 3-fold safety factor was appropriately conservative for methomyl. Input data were provided to address the Safety Factor Committee's review questions, and the committee's report indicated a thorough and careful review. That report provided justification for reducing the 10-fold safety factor to 3-fold by referring to sections of the source reports. Regarding the data gap for acute and subchronic neurotoxicity studies in rats that was the reason for the 3-fold safety factor, the reviewer noted that the gap did not seem to be a pressing need, because similar data were available for two other species, dogs and rabbits. His opinion was that if EPA had been willing to accept the data for dogs and rabbits as an alternative to the rat data, the safety factor might have been removed. The lack of a cumulative risk assessment in this case was not likely a problem, the reviewer said, because of the short half-life of the chemical, meaning that it would dissipate rapidly.

Phosmet

Description

Phosmet is a member of the largest class of insecticides, the organophosphates. It is a broad-spectrum insecticide that causes systemic toxicity by inhibiting cholinesterase, and there also have been concerns about carcinogenicity. Phosmet is marketed for agricultural uses, nonagricultural occupational uses, and homeowner uses to control pests, including moths, beetles, weevils, lice, flies, fleas, and ticks. It is used on a variety of fruit and vegetable crops (especially apples and peaches), tree crops, nut trees, cotton, and ornamentals and in forestry. In addition, phosmet is used for direct animal treatments on cattle, swine, and dogs (flea and tick treatments). There are 43 current food use tolerances for phosmet, of which 1 has been revoked voluntarily during the course of the review. The remainder have yet to be reassessed, pending the required cumulative assessment for the organophosphates.

FQPA Review History

The Safety Factor Committee has reviewed phosmet twice since the law passed in 1996. The first review was through what OPP calls its "OP [Organophosphate] Marathon Meetings," in which all of the organophosphate pesticides, including phosmet, were reviewed together. The Safety Factor Committee held its marathon meeting on June 15 and 16, 1998. In the case of phosmet, it concurred with the findings of the May 1998

toxicology review committee marathon meeting and recommended a 3-fold FQPA safety factor, based on data gaps noted by the toxicology group.[2] Specifically, the marathon meetings found that there was no evidence of increased susceptibility to phosmet in young animals, but there were data gaps for two types of neurotoxicity studies, and the requirement for a developmental neurotoxicity study would depend on the results of those other studies. Because no data were available to assess neurotoxicity, cholinesterase inhibition, behavioral effects, or neuropathology for phosmet, the 3-fold safety factor was recommended.

The second review of phosmet took place in summer 1999 after the registrant submitted new data, including the acute and subchronic neurotoxicity studies. On the basis of the results of these studies and additional information from the registrant, the toxicology review committee determined that the developmental neurotoxicity study was not required. The Safety Factor Committee then concluded that there were no remaining data gaps and no evidence of increased susceptibility. The committee reported that adequate actual data, surrogate data, and/or modeling outputs were available to satisfactorily assess dietary food and residential exposures[3] and to provide a screening level of drinking water exposure assessment. Consequently, the committee recommended that the FQPA safety factor be removed.[4]

OPP's regulatory decision agreed with the Safety Factor Committee that no additional FQPA safety factor was needed for phosmet, and the reregistration document was revised to reflect the new data and decisions

[2]There was also a separate toxicology review committee meeting on phosmet on September 4, 1997, as part of phosmet's reregistration process. The discussion covered FQPA requirements, such as data availability and data gaps—specifically, the need for a developmental neurotoxicity study; possible endocrine disruption; and possible human carcinogenic effects. The toxicology review committee recommended a 3-fold safety factor at that time.

[3]There were no chemical-specific data for phosmet to assess potential exposures to children following outdoor residential applications. Therefore the draft Standard Operating Procedures for Residential Exposure Assessments was used with surrogate data. This type of analysis is intended to represent worst-case or screening-level assessments.

[4]Phosmet's potential for causing cancer in humans was also reassessed in 1999 through a separate internal committee process. As a result, phosmet was classified in the category "suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential." This was consistent with the previous classification, and therefore no change was needed in the risk assessment, which already took this level of cancer risk into account.

(see the version of October 7, 1999, and the February 9, 2000, public release version). The risk assessment for phosmet concluded that (1) dietary food and water risks are not a concern, even when combined, from either acute or chronic exposure, (2) risks from residential exposure to treated dogs and garden uses are a concern, especially for toddlers exposed to treated dogs, and (3) there also are concerns for workers handling the pesticide and regarding some ecological hazards (to birds, water, and honey bees). This latest revised risk assessment describes the risks associated with use of phosmet alone, and it may be revised again when EPA has conducted the necessary cumulative assessment for the organophosphates.

Reviewer's Comments

Our reviewer concluded that through repeated reviews and reports, EPA's consideration of the data on phosmet has been very thorough. The Safety Factor Committee reviews followed the standard operating procedures systematically, and decisions on the completeness and reliability of the data and the lack of data gaps were adequately justified. The committee's conclusion that there was no apparent developmental or reproductive toxicity also was adequately justified and supported removal of the 10-fold safety factor. Our reviewer stated that phosmet is rapidly metabolized and degrades quickly under most environmental conditions; therefore it is seldom detected in food or water, and exposures usually are very low. This helps explain why aggregate exposure to phosmet is low. In our reviewer's opinion, calculated exposure of children resulting from contact with treated dogs appeared to be conservative. Regarding the postponed cumulative risk assessment, he noted: "Having worked on the problem of cumulative risk assessment, I realize that issues relating to cumulative risks present a very complex and controversial problem—a problem that is not going to be easily solved. And the solution, when it comes, is not likely to be to anybody's complete satisfaction."

Incidents of human poisoning from phosmet apparently are relatively common, because our reviewer said that phosmet accounts for the largest number of residential exposures to pesticides that result in treatment in a health care facility. But he observed that these incidents are not an indication of unusual toxicity as much as they are a result of incorrect use. Almost all of the poisoning incidents resulted from failure to properly dilute a concentrated formulation of phosmet for use as flea dip treatment for dogs. Regarding the question of whether phosmet is likely to cause cancer, our reviewer noted that the evidence is limited to reports of increased incidences of tumors in mouse livers (which were marginally

statistically significant) and that there are differences of opinion as to the relevance of increased mouse liver tumors to human health risks.

GAO Contact and Staff Acknowledgments

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Staff Acknowledgments

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